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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/630,967	07/31/2003	Shigeki Ohta	16601-026001	1847
26181	7590	03/20/2006	EXAMINER	
FISH & RICHARDSON P.C. PO BOX 1022 MINNEAPOLIS, MN 55440-1022			GAMETT, DANIEL C	
			ART UNIT	PAPER NUMBER
			1647	

DATE MAILED: 03/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<p align="center">Office Action Summary</p>	Application No. 10/630,967	Applicant(s) OHTA ET AL.	
	Examiner Daniel C. Gamett, PhD	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 December 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-57 is/are pending in the application.
- 4a) Of the above claim(s) 27 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-26 and 38-57 is/are rejected.
- 7) ☒ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 1-57 are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 31 July 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>9/15/03, 12/12/03</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Applicant's election without traverse of claims 5-26 and 38-57 in the reply filed on 12/14/2005 is acknowledged.
2. Claims 27-37 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 12/14/2005.
3. Claims 5-26, 38-57 and linking claims 1-4, insofar as they read upon the elected *in vivo* methods, are under consideration in this office action.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 1-13, 15, 16, 38-44, and 53-56 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent No. 6,242,563, issued June 5, 2001 (of record on IDS filed 09/15/2003). The claims are drawn to methods comprising administration of PACAP to a patient. The '563 patent teaches (throughout) PACAP38, PACAP27 (as in instant claims 15, 16, 40, and 41), and analogs thereof that are agonists of the PACAP receptor. Claims 19-22 of the '563 patent teach methods of treatment that comprise administration of PACAP to the same patient

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population as recited in instant claims 7-12, 42-44, and 53-56. Parenteral administration (as in instant claim 6) is taught in the '563 patent at column 7, lines 29-43. The intended outcomes recited in the instant claims, e.g. increasing stem cell number (claims 1-4) or enhancing differentiation (claim 38) reflect inherent properties of PACAP and would occur whenever the methods of the '563 patent are practiced.

6. Claims 1-13, 15-18, 20, 38-46, 48, and 53-56 are rejected under 35 U.S.C. 102(e) as being anticipated by US 20040038888, filed May 2, 2003, with priority to May 2, 2002. US 20040038888 teaches (throughout) administration of PACAP for treatment of CNS disorders. PACAP is taught to work by "stimulating ependymal cells and subventricular zone cells to proliferate, migrate, differentiate and survive into the desired neural phenotype" [0140], thereby anticipating the intended outcomes recited in claims 1-4 and 38-39, and the cell location limitations of claims 5, 13, and 56. The diseases and disorders taught at [0132] and [0138] clearly indicate adult humans as subjects of treatment (see also [0139]) thereby anticipating instant claims 5-9 and 42-44, and they include all of the diseases recited in instant claims 10-12 and 53-55. Both PACAP38 and PACAP 27 are taught [0073], thereby anticipating claims 15, 16, 40 and 41. Use of PACAP together with additional factors is taught at [0141]; EGF and FGF2 are specifically taught at [0196] and [0010], thereby anticipating instant claims 17, 18, 20, 23, 45, 46, and 48.

7. Claims 1-16, 38-44, and 53-57 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 96/09318 (Arimura), published 26 March, 1996. Arimura teaches a method and pharmaceutical preparations for treating or preventing neuronal cell damage in mammals, comprising administering a PACAP, or an agonist, analog or derivative thereof. A patient

population that anticipates that instant claims 7-12, 42-44, and 53-56 is taught by Arimura at page 1, line 13 to page 2, line 9. The routes of administration taught by Arimura (p. 19, line 16 to page 25, line 9) anticipate those recited in instant claim 6. Arimura further teaches protection of transplanted neural cells in the brain (page 18, line 5-6), thereby anticipating instant claims 14 and 57. The intended outcomes recited in the instant claims, e.g. increasing stem cell number (claims 1-4) or enhancing differentiation (claim 38) reflect inherent properties of PACAP and would occur whenever the methods of WO 96/09318 are practiced.

8. Claims 1-16, 38-44, and 53-57 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent No. 6680295, filed May 21, 1997, which is the same disclosure as WO 96/09318.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 21 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 20040038888 as applied to claims 1-13, 15-18, 20, 38-46, 48, and 53-56 above, and further in view of WO 2003040310, published May 15, 2003 (of record on IDS filed 09/15/2003). As noted above, US 20040038888 teaches, at [0196], use of PACAP together with EGF, thus anticipating claims 20 and 48. US 20040038888 does not, however, teach the specific variants of EGF, namely EGF51N and EGF51Q, recited in dependent claims 21 and 49. WO 2003040310, teaches that these EGF variants retain EGF activity and are more resistant to protease degradation following administration to a subject (page 15, first full paragraph, and Figure 1).

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The retained EGF activity supports the expectation that EGF51N and EGF51Q could be used successfully and the increased stability would motivate one of skill in the art at the time the invention was made to modify the method taught in US 20040038888 to include EGF51N and EGF51Q. It is further noted that the priority document for the instant application, Provisional application 60/399,390, does not teach EGF51N or EGF51Q. Therefore, the priority date for instant claims 21 and 49 is 07/31/2003.

11. Claims 19 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 20040038888 as applied to claims 1-13, 15-18, 20, 23, 38-46, 48, and 53-56 above, and further in view of Whittemore *et al.*, Exp Cell Res. 1999 Oct 10;252(1):75-95 and Schlessinger *et al.*, Molecular Cell. 2000 Sep;6(3):743-50. As noted above, US 20040038888 teaches use of PACAP together with FGF-2, thus anticipating claims 18 and 46. US 20040038888 does not, however, teach heparan sulfate as recited in instant claims 19 and 47. Schlessinger *et al.*, citing earlier work, teach that sulfated proteoglycans, such as heparan sulfate, interact with FGF-2 and FGF-2 receptors to facilitate receptor activation (see Introduction, second full paragraph); they specifically teach the crystal structure of the complex. It is a common practice in the art to include heparin in protocols where FGF-2 is used, as exemplified by Whittemore *et al.*, (see table 3). It would have been obvious to one of skill in the art at the time of the invention to use heparin sulfate along with FGF-2, with the motivation of ensuring that a required co-factor for receptor activation is not limiting.

12. Claims 23-26, 51, and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 20040038888 as applied to claims 1-13, 15-18, 20, 38-46, 48, and 53-56 above because

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selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results. See MPEP 2144.04.IV.C.

Double Patenting

13. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 1, 17, and 22-26, and claims 38, 45, and 50-52 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 8, and 9 and 22, 28, and 29, respectively, of copending Application No. 10/231,479. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons. The embodiments of ‘479-9 and ‘479-29 wherein the selected factor is PACAP and instant claims 22 and 50 recite nearly identical methods in which neural stem cells

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are contacted with both prolactin and PACAP. Furthermore, instant claims 22 and 50 are drawn to species of method that comprise administration of prolactin. Therefore, claims 22 and 50 would anticipate generic Claims '479-1, '479-8, '479-22, and '479-28, which are generically drawn to methods that comprise administering prolactin, or prolactin plus an additional factor. Claims 23-26, 51 and 52 are also obvious modifications of the '479 claims because selection of any order of performing process steps is *prima facie* obvious in the absence of new or unexpected results. See MPEP 2144.04.IV.C.

This is a provisional obviousness-type double patenting rejection.

15. Claims 1, 17, 23, and 45 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 31 of U.S. Patent No. 6844312 ('312-31). Although the conflicting claims are not identical, they are not patentably distinct from each other because '312-31 is drawn to a method, which, in certain embodiments, comprises concurrent treatment of a patient with PACAP and a growth factor. The treatment method of '312-31 comprises additional components, and therefore it is a species that would anticipate the instant claims, which are generic.

Conclusion

16. No claims are allowed.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel C Gamett, Ph.D., whose telephone number is 571 272 1853. The examiner can normally be reached on M-F, 8:30-5:00.

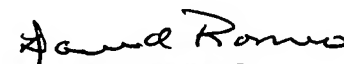
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571 272 0961. The fax phone number for the organization where this application or proceeding is assigned is 571 273 8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

DCG

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14 March 2006


DAVID S. ROMEO
PRIMARY EXAMINER